

A	S(O) <sub>2</sub> E	R <sup>1</sup>
59 		
60 		

By 18. (Twice Amended) A composition comprising a compound according to any one of claims 1-5 or 7-15, in an amount sufficient to inhibit an aspartyl protease; and a pharmaceutically acceptable carrier.

#### REMARKS

Applicants appreciate the Examiner's telephonic discussion of the Action with applicants' agent on January 30, 2002.

Claims 1-5, 7-15, 18-22 and 28 are now pending. Applicants have amended claim 1 to overcome the Examiner's objections (see below). Consistent with the amendments to

claim 1, applicants have canceled claims 16-17 and amended claims 8 and 15 to cancel subject matter not embraced by amended claim 1. Applicants have also amended claim 18 to delete its dependency from canceled claims 16-17.

None of the above amendments adds any new subject matter.

Applicants address the Examiner's rejections and objections individually below.

CLAIM REJECTION - § 112, SECOND PARAGRAPH:

The Examiner has rejected claim 28 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner contends that because claim 28 contains trademarks/trade names, such as "ACYCLOVIR" (line 2) and "VALACICLOVIR" (line 3), the scope of the claim is uncertain because a trademark or trade name only identifies a source of goods and not any particular material or product. Applicants traverse.

"Acyclovir" and "valaciclovir" are not trademarks or trade names. Applicants respectfully submit that "acyclovir" and "valaciclovir" and the like are generic names. These generic names are shown, along with the

corresponding trade names, in Exhibit 2 (printouts of generic/trade name lists from www.dubuisson.co.za, www.merck.com and www.hopkins-aids.edu). The meanings of these commonly accepted expressions are sufficiently precise and well-known to one of skill in the art such that recitation of these generic names does not render the scope of claim 28 indefinite. Accordingly, applicants request that the Examiner withdraw this rejection.

#### OBJECTION TO THE SPECIFICATION

The Examiner has objected to the use of the trademarks "ACYCLOVIR" and "VALACICLOVIR", etc. in the specification and has required that they be capitalized wherever they appear and be accompanied by generic terminology. The Examiner further states that although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort should be made to prevent their use in any manner which might adversely affect their validity as trademarks. Applicants traverse the Examiner's requirement.

As discussed above, "acyclovir" and "valaciclovir" and the like are not trademarks, but are, rather, generic names. Therefore, the present use of these terms in the

specification is proper. Accordingly, applicants request that the Examiner withdraw this objection.

#### CLAIM OBJECTIONS

The Examiner has objected to claims 1-5, 7-22 and 28 for containing an informality. Specifically, the Examiner has objected to the optional substitution on variable A and stated that the elected embodiment for A (tetrahydrofurodihydrofuranyl) should be unsubstituted. Applicants traverse.

During the Examiner's telephonic discussion of the Action with applicants' agent on January 30, 2002, the Examiner has referred to this informality as a search burden. Applicants disagree with the Examiner that a search including optional substituents on tetrahydrofurodihydrofuranyl would be burdensome.

However, the Examiner indicated during the January 30 discussion that she would withdraw this objection if applicants amended claim 1 as set forth in the Office Action (see below). Applicants have amended claim 1 as suggested by the Examiner. Accordingly, applicants respectfully request that the Examiner withdraw these informality objections.

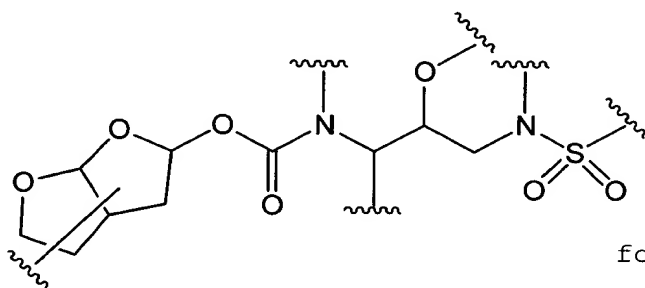
ALLOWABLE SUBJECT MATTER

The Examiner has stated that "upon additional consideration, the Examiner has further limited the generic concept of claim 1". The Examiner contends that a claim to compounds wherein G is H or C<sub>1</sub>-C<sub>4</sub> alkyl and E is aminobenzothiazolyl would be allowable. Applicants traverse.

First, the Examiner has not set forth in the Action any particular reason why only the "further limited generic concept" of claim 1 is allowable. Second, the Examiner's limitation contradicts proper searching practice involving Markush claims. According to the MPEP, proper practice calls for searching on the elected species. If no prior art is found that anticipates or renders obvious the elected species, the prior art search should be extended to the extent necessary to determine the patentability of the Markush-type claim. MPEP § 803.02. The Examiner has not cited any art against claim 1 or any reason that claim 1 is anticipated or rendered obvious. Applicants respectfully submit that applicants are entitled to the entire scope of claim 1, not just the "further limited generic concept" set by the Examiner. To require applicants to limit their generic claim to variable G being H or C<sub>1</sub>-C<sub>4</sub> alkyl and E

being aminobenzothiazolyl unduly limits the breath of applicants' generic claim.

Further, a search on the entire scope of claim 1 is not burdensome. Compounds of claim 1 share a distinct structural nucleus as shown in formula 1 and share a common



formula 1

utility (inhibiting aspartyl protease). A search on formula 1 will necessarily reveal any art relating to compounds of claim 1.

Nevertheless, to expedite prosecution, applicants have amended claim 1 to recite compounds wherein G is H or C<sub>1</sub>-C<sub>4</sub> alkyl and E is optionally substituted aminobenzothiazolyl, as suggested by the Examiner. Consistent with this amendment, applicants have deleted the superfluous recitation of R<sup>4</sup> from amended claim 1. Applicants expressly reserve the right to file divisional or continuing applications directed to the canceled subject matter and claiming priority herefrom under 35 U.S.C. § 120.

Applicants' claim 1 is therefore in compliance with the Examiner's "further limited generic concept" of variables G and E.

CONCLUSION

In view of the foregoing remarks, applicants request that the Examiner favorably reconsider this application and allow the claims pending herein. If the Examiner believes that a telephone conference would expedite allowance of this application, she is invited to telephone applicants' attorneys or agent at (212)596-9000 at any time.

Respectfully submitted,



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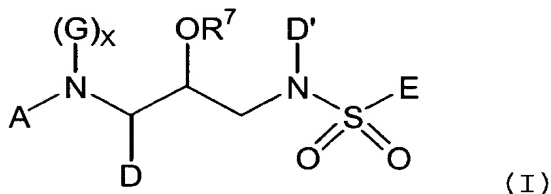
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## APPENDIX OF AMENDMENTS

IN THE CLAIMS

1. (Twice Amended) A compound of the formula (I):



and pharmaceutically acceptable salts thereof; wherein:

A is tetrahydrofurodihydrofuranyl-O-C(O)-, wherein tetrahydrofurodihydrofuranyl is optionally substituted with one or more substituents independently selected from oxo, -OR<sup>2</sup>, SR<sup>2</sup>, -R<sup>2</sup>, -N(R<sup>2</sup>)(R<sup>2</sup>), -R<sup>2</sup>-OH, -CN, -CO<sub>2</sub>R<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, -S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sup>2</sup>, -N(R<sup>2</sup>)-C(O)O-R<sup>2</sup>, -C(O)-R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>, -S(O)<sub>n</sub>-Q, methylenedioxy, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, -NO<sub>2</sub>, Q, -OQ, -OR<sup>7</sup>, -SR<sup>7</sup>, -R<sup>7</sup>, -N(R<sup>2</sup>)(R<sup>7</sup>) or -N(R<sup>7</sup>)<sub>2</sub>;

each Ht is independently selected from C<sub>3</sub>-C<sub>7</sub> cycloalkyl; C<sub>5</sub>-C<sub>7</sub> cycloalkenyl; C<sub>6</sub>-C<sub>14</sub> aryl; or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, N(R<sup>2</sup>), O, S and S(O)<sub>n</sub>; wherein said aryl or said heterocycle is optionally fused to Q; and wherein any member of said Ht is optionally substituted with one or more substituents independently selected from oxo, -OR<sup>2</sup>, SR<sup>2</sup>, -R<sup>2</sup>, -N(R<sup>2</sup>)(R<sup>2</sup>), -R<sup>2</sup>-OH, -CN, -CO<sub>2</sub>R<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, -S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sup>2</sup>, -N(R<sup>2</sup>)-C(O)O-R<sup>2</sup>, -C(O)-R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>, -S(O)<sub>n</sub>-Q, methylenedioxy, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, -NO<sub>2</sub>, Q, -OQ, -OR<sup>7</sup>, -SR<sup>7</sup>, -R<sup>7</sup>, -N(R<sup>2</sup>)(R<sup>7</sup>) or -N(R<sup>7</sup>)<sub>2</sub>;

each R<sup>2</sup> is independently selected from H, or C<sub>1</sub>-C<sub>4</sub> alkyl optionally substituted with a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; or a 5-7 membered saturated, partially saturated or unsaturated heterocyclic ring containing one or more



heteroatoms selected from O, N, S,  $S(O)_n$  or  $N(R^{33})$ ; wherein any of said ring systems or  $N(R^{33})$  is optionally substituted with 1 to 4 substituents independently selected from  $-X'-Y'$ ,  $-O$ -arylalkyl,  $-S$ -arylalkyl,  $-N(Y')_2$ ,  $-N(H)$ -arylalkyl,  $-N(C_1-C_4 \text{ alkyl})$ -arylalkyl, oxo,  $-O-(C_1-C_4 \text{ alkyl})$ , OH,  $C_1-C_4$  alkyl,  $-SO_2H$ ,  $-SO_2-(C_1-C_4 \text{ alkyl})$ ,  $-SO_2-NH_2$ ,  $-SO_2-NH(C_1-C_4 \text{ alkyl})$ ,  $-SO_2-N(C_1-C_4 \text{ alkyl})_2$ ,  $-NH_2$ ,  $-NH(C_1-C_4 \text{ alkyl})$ ,  $-N(C_1-C_4 \text{ alkyl})_2$ ,  $-NH-C(O)H$ ,  $-N(C_1-C_4 \text{ alkyl})-C(O)H$ ,  $-NH-C(O)-C_1-C_4 \text{ alkyl}$ ,  $-C_1-C_4 \text{ alkyl}-OH$ ,  $-OH$ ,  $-CN$ ,  $-C(O)OH$ ,  $-C(O)O-C_1-C_4 \text{ alkyl}$ ,  $-C(O)-NH_2$ ,  $-C(O)-NH(C_1-C_4 \text{ alkyl})$ ,  $-C(O)-N(C_1-C_4 \text{ alkyl})_2$ , halo or  $-CF_3$ ;

$X'$  is  $-O-$ ,  $-S-$ ,  $-NH-$ ,  $-NHC(O)-$ ,  $-NHC(O)O-$ ,  $-NHSO_2-$ , or  $-N-(C_1-C_4 \text{ alkyl})-$ ;

$Y'$  is  $C_1-C_{15}$  alkyl,  $C_2-C_{15}$  alkenyl or alkynyl, wherein one to five carbon atoms in  $Y'$  are optionally substituted with  $C_3-C_7$  cycloalkyl or  $C_5-C_6$  cycloalkenyl,  $C_6-C_{14}$  aryl or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, NH, O, S and  $S(O)_n$ ;

each  $R^3$  is independently selected from H, Ht,  $C_1-C_6$  alkyl,  $C_2-C_6$  alkenyl,  $C_2-C_6$  alkynyl,  $C_3-C_6$  cycloalkyl or  $C_5-C_6$  cycloalkenyl; wherein any member of said  $R^3$ , except H, is optionally substituted with one or more substituents selected from  $-OR^2$ ,  $-C(O)-N(R^2)_2$ ,  $-S(O)_n-N(R^2)_2$ ,  $-N(R^2)_2$ ,  $-N(R^2)-C(O)O(R^2)$ ,  $-N(R^2)-C(O)N(R^2)_2$ ,  $-N(R^2)-C(O)-R^2$ , Ht,  $-CN$ ,  $-SR^2$ ,  $-C(O)OR^2$ , or  $N(R^2)-C(O)-R^2$ ;

each  $R^{33}$  is selected from H,  $C_1-C_6$  alkyl,  $C_2-C_6$  alkenyl,  $C_2-C_6$  alkynyl,  $C_3-C_6$  cycloalkyl or  $C_5-C_6$  cycloalkenyl,  $C_6-C_{14}$  aryl or a 5-7 membered saturated or unsaturated heterocycle, containing one or more heteroatoms selected from N, NH, O, S and  $S(O)_n$ ;

each  $n$  is independently 1 or 2;

$G$  is selected from  $H[, R^7]$  or  $C_1-C_4$  alkyl;

$x$  in  $(G)_x$  is 1;

D is C<sub>1</sub>-C<sub>6</sub> alkyl substituted with Q, wherein said alkyl is optionally substituted with one or more groups selected from C<sub>3</sub>-C<sub>6</sub> cycloalkyl, -R<sup>3</sup>, -O-Q or Q;

each Q is independently selected from a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; wherein Q contains one substituent selected from -OR<sup>2</sup>, -OR<sup>8</sup>, -O-arylalkyl, -SR<sup>8</sup>, -S-arylalkyl, -N(R<sup>2</sup>)R<sup>8</sup>, -N(R<sup>2</sup>)-arylalkyl and may be optionally substituted with one or more additional substituents independently selected from oxo, -OR<sup>8</sup>, -O-arylalkyl, -SR<sup>8</sup>, -S-arylalkyl, -N(R<sup>2</sup>)R<sup>8</sup>, -N(R<sup>2</sup>)-arylalkyl, -OR<sup>2</sup>, -R<sup>2</sup>, -SO<sub>2</sub>R<sup>2</sup>, -SO<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sup>2</sup>, -OH, (C<sub>1</sub>-C<sub>4</sub>)-OH, -CN, -CO<sub>2</sub>R<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, halo or -CF<sub>3</sub>;

each R<sup>8</sup> is independently selected from Ht', -C<sub>1</sub>-C<sub>15</sub> branched or straight chain alkyl, alkenyl or alkynyl wherein one to five carbon atoms in said alkyl, alkenyl or alkynyl are independently replaced by W, or wherein one to five carbon atoms in said alkyl, alkenyl or alkynyl are substituted with Ht'; and wherein R<sup>8</sup> is additionally and optionally substituted with one or more groups independently selected from -OH; -S(C<sub>1</sub>-C<sub>6</sub> alkyl); -CN; -CF<sub>3</sub>; -N(R<sup>2</sup>)<sub>2</sub>; halo; -C<sub>1</sub>-C<sub>4</sub>-alkyl; -C<sub>1</sub>-C<sub>4</sub>-alkoxy; -Ht'; -O-Ht'; -NR<sup>2</sup>-CO-N(R<sup>2</sup>)<sub>2</sub>; -CO-N(R<sup>2</sup>)<sub>2</sub>; -R<sup>1</sup>-C<sub>2</sub>-C<sub>6</sub> alkenyl, which is optionally substituted with one or more groups independently selected from hydroxy, C<sub>1</sub>-C<sub>4</sub> alkoxy, -Ht', -O-Ht', -NR<sup>2</sup>-CO-N(R<sup>2</sup>)<sub>2</sub> or -CO-N(R<sup>2</sup>)<sub>2</sub>; or R<sup>7</sup>;

wherein W is -O-, -NR<sup>2</sup>-, -S-, -C(O)-, -C(S)-, -C(=NR<sup>2</sup>)-, -S(O)<sub>2</sub>-, -NR<sup>2</sup>-S(O)<sub>2</sub>-, -S(O)<sub>2</sub>-NR<sup>2</sup>-, -NR<sup>2</sup>-C(O)O-, -O-C(O)NR<sup>2</sup>-, -NR<sup>2</sup>-C(O)NR<sup>2</sup>-, -NR<sup>2</sup>-C(S)NR<sup>2</sup>-, -CONR<sup>2</sup>, -NR<sup>2</sup>C(O)-, -C(S)NR<sup>2</sup>, -NR<sup>2</sup>C(S)-, -NR<sup>2</sup>-C(=N-CN)-NR<sup>2</sup>-, -NR<sup>2</sup>C(=N-CN)O- or -C(O)O-;

each Ht' is independently selected from C<sub>3</sub>-C<sub>7</sub> cycloalkyl; C<sub>5</sub>-C<sub>7</sub> cycloalkenyl; C<sub>6</sub>-C<sub>14</sub> aryl; 5-7 membered saturated or unsaturated heterocycle containing one or more

heteroatoms selected from N,  $N(R^2)$ , O, S and  $S(O)_n$ ; wherein said aryl or said heterocycle is optionally fused to  $Q'$ ; and wherein any member of said Ht' is optionally substituted with one or more substituents independently selected from oxo,  $-OR^2$ ,  $SR^2$ ,  $-R^2$ ,  $-N(R^2)(R^2)$ ,  $-R^2-OH$ ,  $-CN$ ,  $-CO_2R^2$ ,  $-C(O)-N(R^2)_2$ ,  $-S(O)_2-N(R^2)_2$ ,  $-N(R^2)-C(O)-R^2$ ,  $-N(R^2)-C(O)O-R^2$ ,  $-C(O)-R^2$ ,  $-S(O)_n-R^2$ ,  $-OCF_3$ ,  $-S(O)_n-Q'$ , methylenedioxy,  $-N(R^2)-S(O)_2(R^2)$ , halo,  $-CF_3$ ,  $-NO_2$ ,  $Q'$ ,  $-OQ'$ ,  $-OR^7$ ,  $-SR^7$ ,  $-R^7$ ,  $-N(R^2)(R^7)$  or  $-N(R^7)_2$ ;

each  $Q'$  is independently selected from a 3-7 membered saturated, partially saturated or unsaturated carbocyclic ring system; or a 5-7 membered saturated, partially saturated or unsaturated heterocyclic ring containing one or more heteroatoms selected from O, N, S,  $S(O)_n$  or  $N(R^2)$ ;

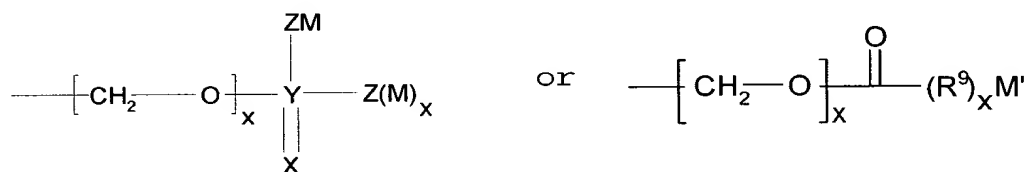
$D'$  is selected from  $C_1-C_{15}$  alkyl,  $C_1-C_{15}$  alkoxy,  $C_2-C_{15}$  alkenyl,  $C_2-C_{15}$  alkenyloxy,  $C_2-C_{15}$  alkynyl, or  $C_2-C_{15}$  alkynyloxy, wherein  $D'$  optionally comprises one or more substituents independently selected from Ht, oxo, halo,  $-CF_3$ ,  $-OCF_3$ ,  $-NO_2$ , azido,  $-SH$ ,  $-SR^3$ ,  $-N(R^3)-N(R^3)_2$ ,  $-O-N(R^3)_2$ ,  $-(R^3)N-O-(R^3)$ ,  $-N(R^3)_2$ ,  $-CN$ ,  $-CO_2R^3$ ,  $-C(O)-N(R^3)_2$ ,  $-S(O)_n-N(R^3)_2$ ,  $-N(R^3)-C(O)-R^3$ ,  $-N(R^3)-C(O)-N(R^3)_2$ ,  $-C(O)-R^3$ ,  $-S(O)_n-R^3$ ,  $-N(R^3)-S(O)_n(R^3)$ ,  $-N(R^3)-S(O)_n-N(R^3)_2$ ,  $-S-NR^3-C(O)R^3$ ,  $-C(S)N(R^3)_2$ ,  $-C(S)R^3$ ,  $-NR^3-C(O)OR^3$ ,  $-O-C(O)OR^3$ ,  $-O-C(O)N(R^3)_2$ ,  $-NR^3-C(S)R^3$ ,  $=N-OH$ ,  $=N-OR^3$ ,  $=N-N(R^3)_2$ ,  $=NR^3$ ,  $=NNR^3C(O)N(R^3)_2$ ,  $=NNR^3C(O)OR^3$ ,  $=NNR^3S(O)_n-N(R^3)_2$ ,  $-NR^3-C(S)OR^3$ ,  $-NR^3-C(S)N(R^3)_2$ ,  $-NR^3-C[=N(R^3)]-N(R^3)_2$ ,  $-N(R^3)-C[=N-NO_2]-N(R^3)_2$ ,  $-N(R^3)-C[=N-NO_2]-OR^3$ ,  $-OC(O)R^3$ ,  $-OC(S)R^3$ ,  $-OC(O)N(R^3)_2$ ,  $-C(O)N(R^3)-N(R^3)_2$ ,  $-N(R^3)-N(R^3)C(O)R^3$ ,  $-N(R^3)-OC(O)R^3$ ,  $-N(R^3)-OC(O)R^3$ ,  $-N(R^3)-OC(O)R^3$ ,  $-OC(S)N(R^3)_2$ ,  $-OC(S)N(R^3)(R^3)$ , or  $-PO_3-R^3$ ;

$E$  is [selected from Ht; Ht-Ht; Ht fused with Ht;  $-O-R^3$ ;  $-N(R^2)(R^3)$ ;  $C_1-C_6$  alkyl, which is optionally substituted with one or more groups selected from  $R^4$  or Ht;

C<sub>2</sub>-C<sub>6</sub> alkenyl, which is optionally substituted with one or more groups selected from R<sup>4</sup> or Ht; C<sub>3</sub>-C<sub>6</sub> saturated carbocycle, which is optionally substituted with one or more groups selected from R<sup>4</sup> or Ht; or C<sub>5</sub>-C<sub>6</sub> unsaturated carbocycle, which is optionally substituted with one or more groups selected from R<sup>4</sup> or Ht] benzothiazolyl optionally substituted with one or more substituents independently selected from oxo, -OR<sup>2</sup>, SR<sup>2</sup>, -R<sup>2</sup>, -N(R<sup>2</sup>)(R<sup>2</sup>), -R<sup>2</sup>-OH, -CN, -CO<sub>2</sub>R<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, -S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sup>2</sup>, -N(R<sup>2</sup>)-C(O)O-R<sup>2</sup>, -C(O)-R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>, -S(O)<sub>n</sub>-Q, methylenedioxy, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, -NO<sub>2</sub>, Q, -OQ, -OR<sup>7</sup>, -SR<sup>7</sup>, -R<sup>7</sup>, -N(R<sup>2</sup>)(R<sup>7</sup>) or -N(R<sup>7</sup>)<sub>2</sub>;

[each R<sup>4</sup> is independently selected from -R<sup>2</sup>, -OR<sup>2</sup>, -OR<sup>3</sup>, -SR<sup>2</sup>, -SOR<sup>2</sup>, -SO<sub>2</sub>R<sup>2</sup>, -CO<sub>2</sub>R<sup>2</sup>, -OC(O)-R<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, -C(O)-NR<sup>2</sup>(OR<sup>2</sup>), -S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, halo, -NR<sup>2</sup>-C(O)-R<sup>2</sup>, -NR<sup>2</sup>-OR<sup>2</sup>, -N(R<sup>2</sup>)<sub>2</sub> or -CN;]

each R<sup>7</sup> is independently selected from hydrogen,



wherein each M is independently selected from H, Li, Na, K, Mg, Ca, Ba, -N(R<sup>2</sup>)<sub>4</sub>, C<sub>1</sub>-C<sub>12</sub>-alkyl, C<sub>2</sub>-C<sub>12</sub>-alkenyl, or -R<sup>6</sup>; wherein 1 to 4 -CH<sub>2</sub> radicals of the alkyl or alkenyl group, other than the -CH<sub>2</sub> that is bound to Z, is optionally replaced by a heteroatom group selected from O, S, S(O), S(O<sub>2</sub>), or N(R<sup>2</sup>); and wherein any hydrogen in said alkyl, alkenyl or R<sup>6</sup> is optionally replaced with a substituent selected from oxo, -C<sub>1</sub>-C<sub>4</sub> alkyl, -N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)<sub>3</sub>, -OH, -O-(C<sub>1</sub>-C<sub>4</sub> alkyl), -CN, -C(O)OR<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>, S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sub>2</sub>, C(O)R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>, -S(O)<sub>n</sub>-R<sup>6</sup>, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, or -NO<sub>2</sub>;

M' is H, C<sub>1</sub>-C<sub>12</sub>-alkyl, C<sub>2</sub>-C<sub>12</sub>-alkenyl, or -R<sup>6</sup>;  
 wherein 1 to 4 -CH<sub>2</sub> radicals of the alkyl or alkenyl group  
 is optionally replaced by a heteroatom group selected from  
 O, S, S(O), S(O<sub>2</sub>), or N(R<sup>2</sup>); and wherein any hydrogen in  
 said alkyl, alkenyl or R<sup>6</sup> is optionally replaced with a  
 substituent selected from oxo, -OR<sup>2</sup>, -C<sub>1</sub>-C<sub>4</sub> alkyl, -N(R<sup>2</sup>)<sub>2</sub>,  
 N(R<sup>2</sup>)<sub>3</sub>, -OH, -O-(C<sub>1</sub>-C<sub>4</sub> alkyl), -CN, -C(O)OR<sup>2</sup>, -C(O)-N(R<sup>2</sup>)<sub>2</sub>,  
 -S(O)<sub>2</sub>-N(R<sup>2</sup>)<sub>2</sub>, -N(R<sup>2</sup>)-C(O)-R<sub>2</sub>, -C(O)R<sup>2</sup>, -S(O)<sub>n</sub>-R<sup>2</sup>, -OCF<sub>3</sub>,  
 -S(O)<sub>n</sub>-R<sup>6</sup>, -N(R<sup>2</sup>)-S(O)<sub>2</sub>(R<sup>2</sup>), halo, -CF<sub>3</sub>, or -NO<sub>2</sub>;

x, when associated with R<sup>7</sup>, is 0 or 1;

Z is O, S, N(R<sup>2</sup>)<sub>2</sub>, or, when M is not present, H;

Y is P or S;

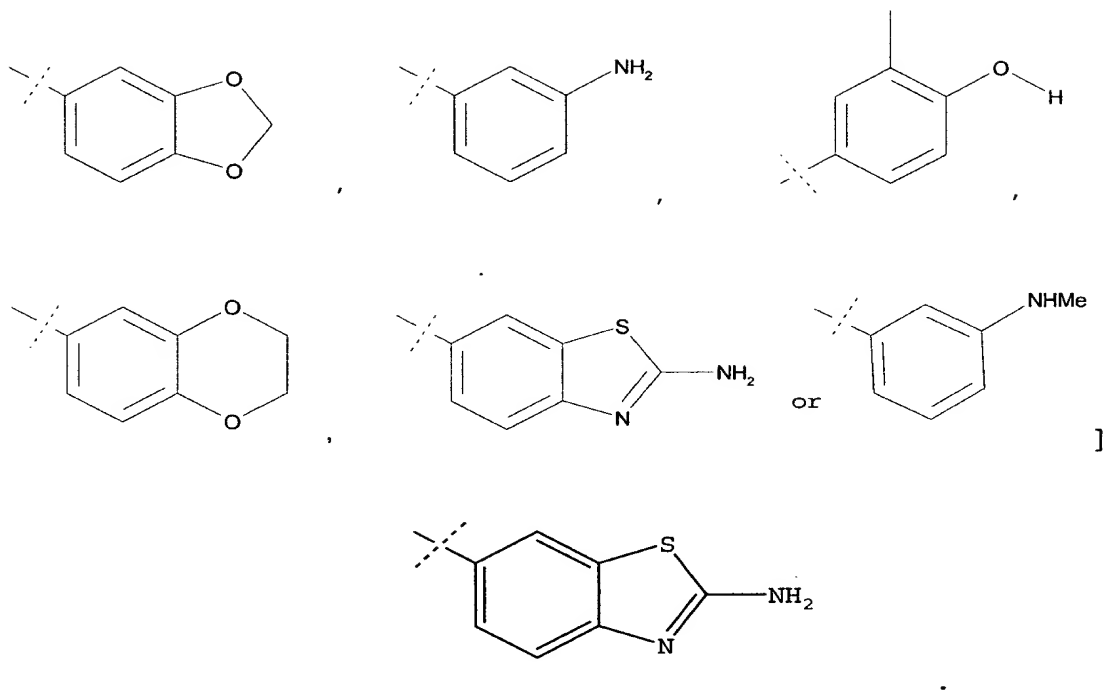
X is O or S;

R<sup>9</sup> is C(R<sup>2</sup>)<sub>2</sub>, O or N(R<sup>2</sup>); wherein when Y is S, Z is  
 not S; and

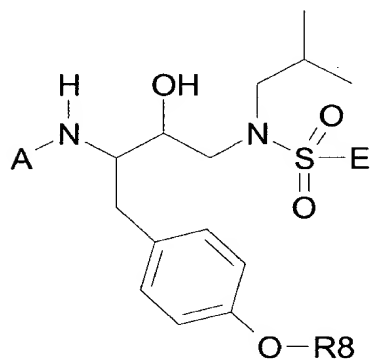
R<sup>6</sup> is a 5-6 membered saturated, partially  
 saturated or unsaturated carbocyclic or heterocyclic ring  
 system, or an 8-10 membered saturated, partially saturated  
 or unsaturated bicyclic ring system; wherein any of said  
 heterocyclic ring systems contains one or more heteroatoms  
 selected from O, N, S, S(O)<sub>n</sub> or N(R<sup>2</sup>); and wherein any of  
 said ring systems optionally contains 1 to 4 substituents  
 independently selected from -OH, -C<sub>1</sub>-C<sub>4</sub> alkyl, -O-(C<sub>1</sub>-C<sub>4</sub>  
 alkyl) or -O-C(O)-(C<sub>1</sub>-C<sub>4</sub> alkyl).

8. (Twice Amended) The compound according to claim  
 1, wherein:

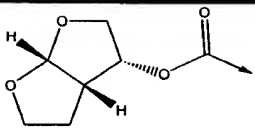
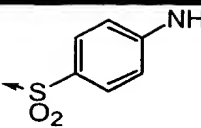
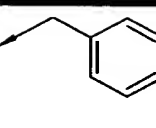
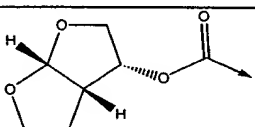
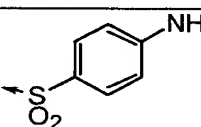
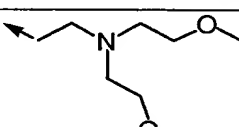
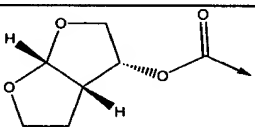
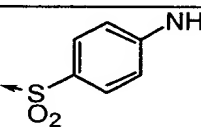
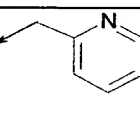
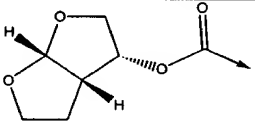
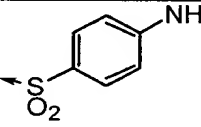
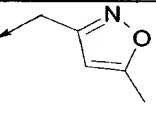
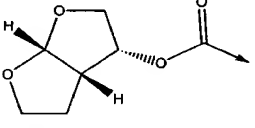
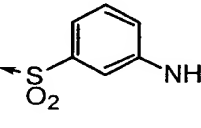
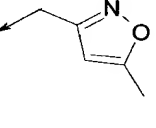
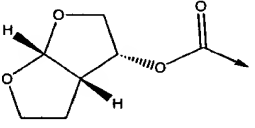
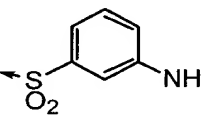
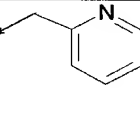
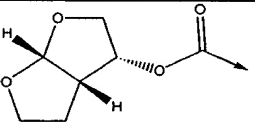
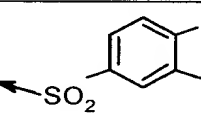
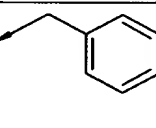
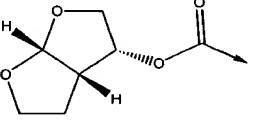
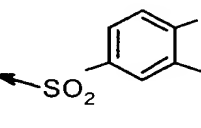
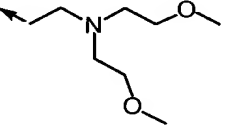
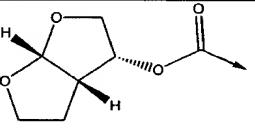
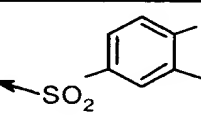
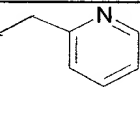
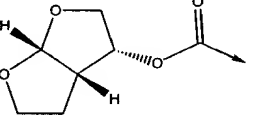
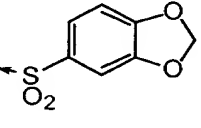
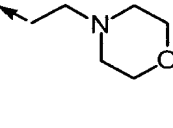
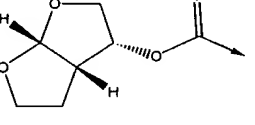
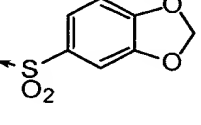
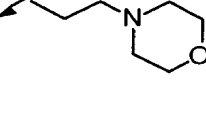
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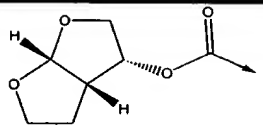
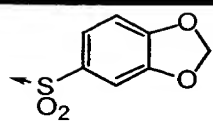
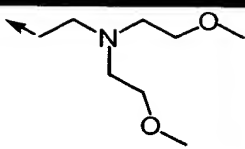
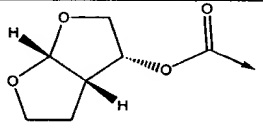
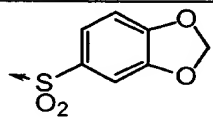
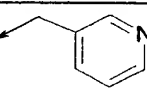
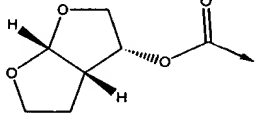
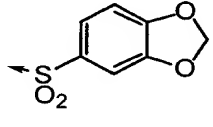
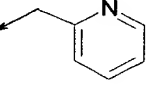
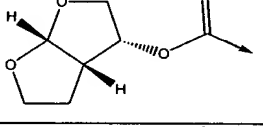
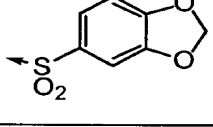
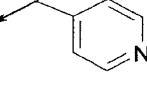
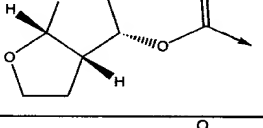
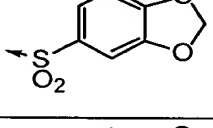
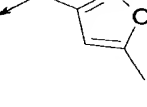
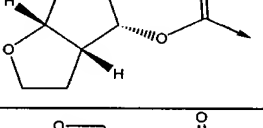
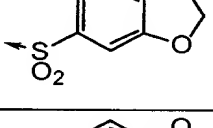
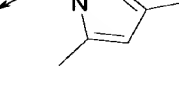
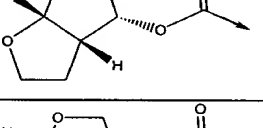
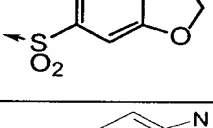

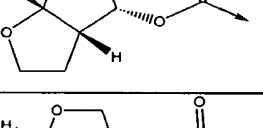
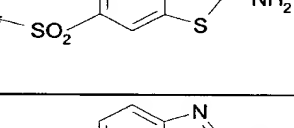
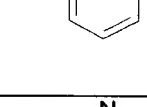
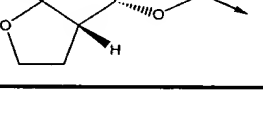
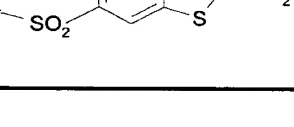
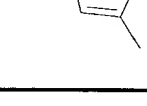


15. (Twice Amended) The compound according to claim 9, wherein said compound is selected from compound numbers: [26, 27, 31, 33, 35, 36, 38, 41, 43, 48, 49, 51, 52, 53, 54, 55, 56, 57,] 59[,] or 60[, 71, 72, 73, 74, 202-204, 209, 213, 215, 217, 223, 227, 231, 233, 236, 237, 239, 243, 247, 250, 260, 263, 271, 281, 289, 293, 295, 304, 309, 317, 319, 320, 322, 334, 335, 348, 364, 367, 368, 375, 382, 383 or 396], wherein said compound is as defined below:

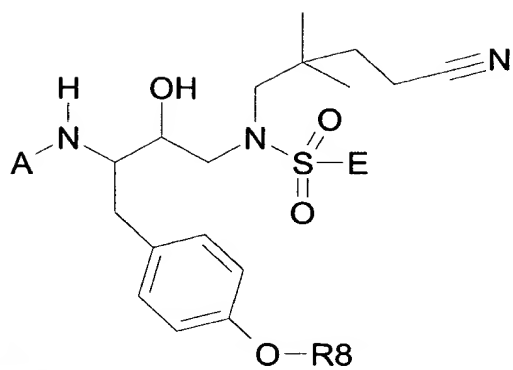


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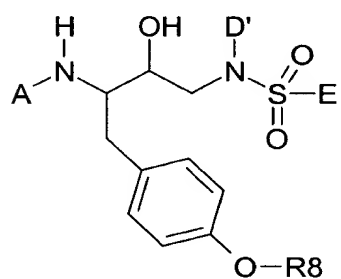
A	$S(O)_2E$	$R^3$
26 		
27 		
31 		
33 		
35 		
36 		
38 		
41 		
43 		
48 		
49 		

A	$S(O)_2E$	$R^3$
51 		
52 		
53 		
54 		
55 		
56 		
57 		
59 		
60 		

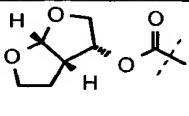
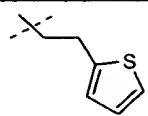

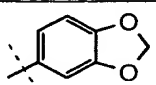
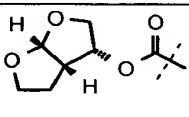
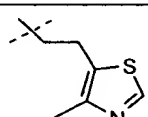

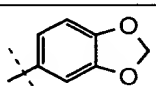
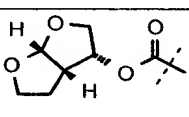
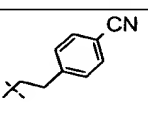

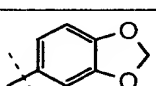
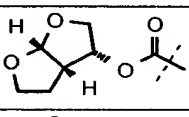
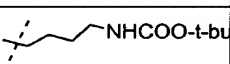

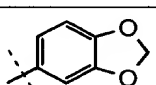
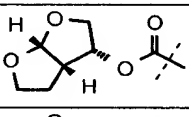
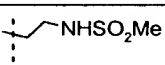

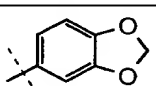
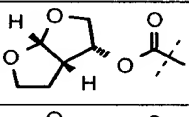
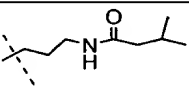

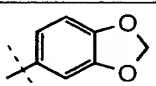
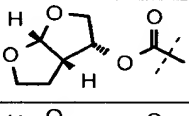
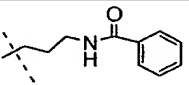

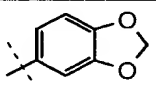
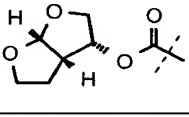
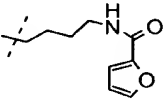

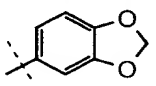
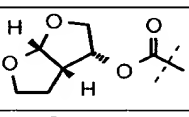
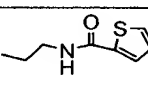

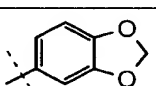
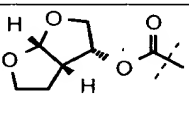
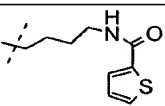

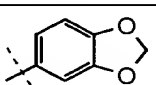
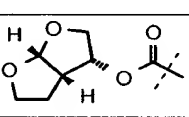
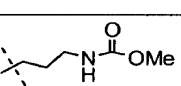

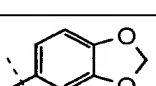
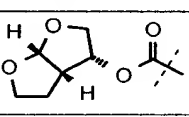
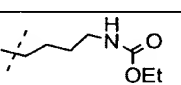

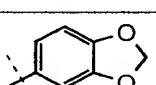
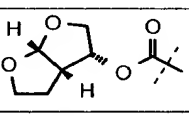
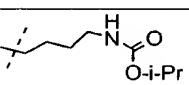

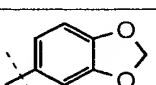
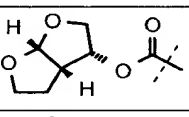
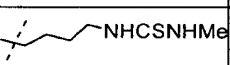

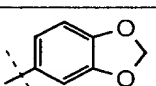
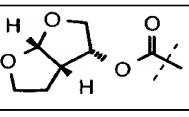
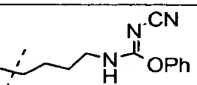

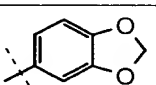




	A	S(O) <sub>2</sub> E	R <sup>8</sup>
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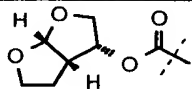
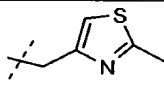

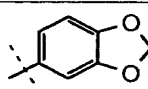
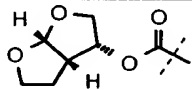
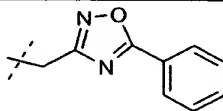

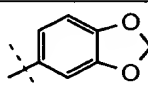
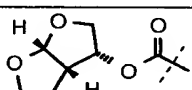
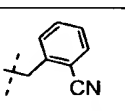

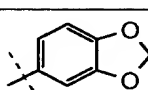
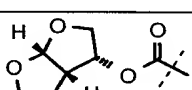
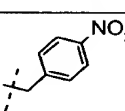

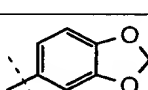
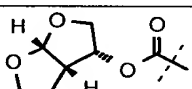
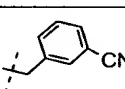
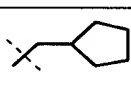
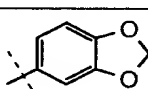


	A	R <sup>8</sup>	D'	E
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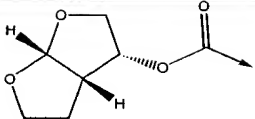
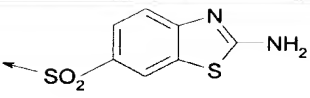

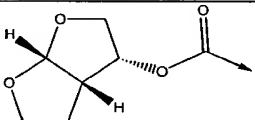
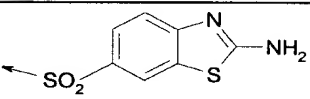
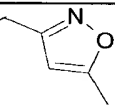
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	A	R <sup>8</sup>	D'	E
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A	$S(O)_2E$	$R^8$
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Claims 16 and 17 have been canceled.

18. (Twice Amended) A composition comprising a compound according to any one of claims 1-5 or [7-17] 7-15, in an amount sufficient to inhibit an aspartyl protease; and a pharmaceutically acceptable carrier.